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Fanconi Syndrome and Oat Cell Carcinoma of the Lung

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THE RENAL TUBULAR DYSFUNCTION associated with Fanconi syndrome* is characterized by the renal wasting of circulating electrolytes, glucose and amino acids in the presence of metabolic acidosis and minimal azotemia.[1,2] In addition to the genetic causes of this malady, various acquired disorders have been identified, principally results of renal toxicity from heavy metals and orally ingested drugs, and from the disorders associated with paraproteinemias.[3,4]

This report presents an instance in which Fanconi syndrome has been related to oat cell carcinoma of the lung.

Report of a Case

A 56-year-old black woman, a domestic worker, was well until May 1976. However, progressively increasing weakness, diffuse body aches and nausea developed and she was admitted to hospital in June.

On physical examination the patient appeared chronically ill and was able to stand only with assistance. Blood pressure was 115/65 mm of mercury with the patient sitting. There was evidence of mild muscle wasting along the temporal regions, the pectoral region and the proximal musculature of the legs. Other findings of the examination were normal.

A routine x-ray study of the chest showed a left upper lobe infiltrate. The hemoglobin value was 13.2 grams per dl, the leukocyte count was 3,500 with 42 percent neutrophils and the platelet count was 98,000 per cu mm. The results of blood chemistry studies and analyses of urine are summarized in Tables 1 and 2. Bronchoscopy with biopsy showed the presence of oat cell carcinoma. Findings on brain, liver and bone scans were normal. A bone marrow biopsy disclosed infiltration with oat cell carcinoma. Electrolyte abnormalities and abnormal results on analysis of urine were noted in the initial laboratory studies, but the causes of these findings were not aggressively pursued. The patient was treated with cyclophosphamide, vincristine and methotrexate. She rapidly regained her strength and normal habitus. A complete remission was achieved approximately nine weeks after diagnosis.

The patient was readmitted to hospital in June 1977 because of weakness, lethargy, tremors, anorexia and general malaise. Examination disclosed pronounced weakness of the musculature and a diffuse tremor. No abnormalities were seen on an x-ray film of the chest and a liver scan. A bone scan showed increased vertebral uptake. Blood

*THE WESTERN JOURNAL'S style regarding eponyms is that they are not written in the possessive form; therefore Graves disease, Ewing sarcoma and Paget disease. A explanation may be found on page 78 of the July 1978 issue.

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TABLE 1.—*Results of Blood Chemistry Studies in Patient With Oat Cell Lung Carcinoma and Renal Tubular Dysfunction*

	June 1976	*June 1977*	*October 1977*	*November 1977*
Body surface area (sq m)	1.87	...	...	...
Plasma urate (mg/dl)	2.8	1.6	1.7	4.7
Plasma glucose (mg/dl)	76.0	54.0	45.0	86.0
Serum cholesterol (mg/dl)	258.0	221.0	218.0	254.0
Blood urea nitrogen (mg/dl)	13.0	11.0	20.0	11.0
Creatinine (mg/dl)	0.7	0.6	0.6	1.0
Serum phosphorus (mg/dl)	2.2	1.1	1.9	3.4
Serum calcium (mg/dl)	9.4	8.7	8.8	9.4
Serum albumin (grams/dl)	3.7	3.5	3.3	3.8
Serum sodium (mEq/liter)	132.0	128.0	112.0	141.0
Serum potassium (mEq/liter)	3.1	2.1	2.1	4.4
Serum carbon dioxide (mEq/liter)	19.0	17.0	18.0	25.0
Serum chloride (mEq/liter)	112.0	106.0	98.0	102.0

TABLE 2.—*Results of Analyses of Urine in Patient With Oat Cell Lung Carcinoma and Renal Tubular Dysfunction*

	June 1976	*June 1977*	*October 1977*	*November 1977*
24-hour glucose (mg)	...	570	512	224
Clinitest	1+	3+	3+	1+
Ketone	1+	1+	2+	0
Protein	1+	1+	1+	0
T_m phosphorus (% filtered load)	...	...	32%	61%
Amino acids (grams/24 hours)	...	2.2	2.6	1.4
24-hour urinary sodium/potassium (mEq/liter)	116/88	88/96	113/108	90/46
Urinary urate (mg/24 hours)	...	622	560	324
T_m PAH (mg/mm)	...	88	85	77
C_{in} (ml/mm)	...	121	106	113
C_{PAH} (ml/mm)	...	605	581	560

C_{in} = insulin clearance C_{PAH} = para-aminohippurate clearance PAH = para-aminohippuric acid
T_m = maximal tubular excretory capacity

chemistry studies disclosed a metabolic acidosis with hyponatremia, hypokalemia, hypophosphatemia and a subnormal uric acid titer. Analysis of urine showed glycosuria, proteinuria and aminoaciduria. Renal evaluation disclosed the presence of normal glomerular and tubular secretory function, although the quantities of sodium, potassium, uric acid, amino acids and glucose delivered through the urine were abnormally high. The patient was given therapy with citrate of potassium and potassium phosphate. Chemotherapy was altered to include doxorubicin and CCNU (chloroethyl cyclohexyl nitrosourea [lomustine]). Serum chemistry values improved although the urinary abnormalities persisted. The tremors and weakness subsided.

Another admission was necessitated in October 1977, heralded by diffuse muscle aches, severe weakness, headaches, cervical spinal pain and dyspnea. An x-ray study of the chest showed a mass in the left lung extending into the mediastinum. A bone scan indicated progression of osseous disease. Laboratory data mirrored those present in October 1977. Serum immunoelectrophoresis was normal. Urine immunoelectrophoresis showed no abnormal gammaglobulins. A study of urine for heavy metals showed no abnormal levels. Rheumatoid factor, latex fixation titer, lupus erythematosus preparation, cold agglutinins and C3 complement titer were normal. Additional chemotherapy was instituted with vinblastine, procarbazine and megadoses of methotrexate with folinic acid rescue. A partial remission was obtained with resolution of the pulmonary mass, lessening of bone pain, and decrease of weakness and tremors. The electrolyte abnormalities again improved when potassium citrate and potassium phosphate were given. The improved status continued until January 1978 when Gram-negative septicemia occurred during a period of pancytopenia and the patient died.

Discussion

It is uncertain whether the patient had renal tubular dysfunction antedating the occurrence of the oat cell carcinoma. However, the absence of previous symptoms, the initially normal findings on roentgenograms and the patient's initially normal habitus was inconsistent with chronic Fanconi syndrome.[1] An autopsy was not permitted, and therefore the presence or absence of an anatomic defect can only be theorized. However, it is possible that the cause of the renal tubular dysfunction was the presence of an unidentified toxin, probably produced by the neoplasm, being deposited in the renal tubular parenchyma and affecting normal reabsorptive mechanisms. Our studies of the immediate family of this patient were limited to serum electrolyte studies and analyses of urine; however, these persons are in good health and laboratory studies show no abnormalities.

Summary

A case of a patient with oat cell carcinoma of the lung and concomitant Fanconi syndrome is presented. Evidence suggests that the renal tubular dysfunction was acquired and became symptomatic during the presence of the neoplasm.

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